

## CLAIMS

What is claimed is:

- 1) A method of determining the pH of a sample, comprising:
  - a) Determining an infrared spectrum of the sample;
  - b) Determining the concentration of hemoglobin of the sample;
  - c) Selecting a model relating an infrared spectrum to pH that is applicable for samples having the determined hemoglobin concentration;
  - d) Determining the pH of the sample from the infrared spectrum and the selected model.
- 2) A method as in Claim 1, wherein the model comprises regression coefficients relating an infrared spectrum to sample pH.
- 3) A method as in Claim 1, wherein the model comprises a model determined from calibration data collected from samples with hemoglobin levels spanning the range of sample hemoglobin levels.
- 4) A method as in Claim 1, wherein the model comprises a model determined from hemoglobin-specific regression coefficients applied to calibration data collected from samples with hemoglobin levels that do not span the sample hemoglobin range.
- 5) A method as in Claim 1, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in at least one of transmission, diffuse reflectance, transmittance, ATR.
- 6) A method as in Claim 1, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in at least one of transmission, diffuse reflectance, transmittance, ATR.
- 7) A method as in Claim 1, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 4000 – 25000 cm<sup>-1</sup>.
- 8) A method as in Claim 1, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 4000 – 8000 cm<sup>-1</sup>.
- 9) A method as in Claim 1, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 6000 – 6500 cm<sup>-1</sup>.
- 10) A method as in Claim 1, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation at a spectral resolution of 64 cm<sup>-1</sup> or finer.
- 11) A method as in Claim 1, wherein determining the concentration of hemoglobin comprises at least one of:

- a) Direct measurement of a blood sample using an external instrument or method;
  - b) Spectroscopic measurement of a blood sample; and
  - c) Noninvasive measurement of perfused tissue.
- 12) A method as in Claim 1, wherein determining the concentration of hemoglobin comprises at least one of:
- a) Measuring the sample hemoglobin concentration under physiological conditions that are not undergoing rapid change;
  - b) Accounting for errors introduced by potentially interfering intravascular substances.
- 13) A method as in Claim 1, wherein the sample comprises at least one of:
- a) A blood sample drawn from the patient;
  - b) A blood sample measured intravascularly (indwelling measurement);
  - c) Perfused tissue;
  - d) Perfused skin;
  - e) An ex vivo blood sample in a transmission vessel;
  - f) An ex vivo blood sample in a transfectance vessel;
  - g) A blood sample in an on-line flow circuit;
  - h) In situ measurement of a perfused tissue; and
  - i) In situ measurement of a perfused organ or muscle.
- 14) A method of determining pH of a sample, comprising:
- a) Determining an infrared spectrum of the sample;
  - b) Verifying that the spectrum is spectrally consistent with the calibration model;
  - c) Determining the concentration of hemoglobin of the sample;
  - d) Determining the pH of the sample from the infrared spectrum, the determined hemoglobin, hematocrit, or equivalent concentration, and a model relating an infrared spectrum and associated hemoglobin concentration to pH.
- 15) A method as in Claim 14, wherein the model comprises regression coefficients relating an infrared spectrum to sample pH.
- 16) A method as in Claim 14, wherein the model comprises a model determined from calibration data collected from samples with hemoglobin levels spanning the range of sample hemoglobin levels.
- 17) A method as in Claim 14, wherein the model comprises a model determined from hemoglobin-specific regression coefficients applied to calibration data collected from samples with hemoglobin levels that do not span the sample hemoglobin range.

- 18) A method as in Claim 14, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in at least one of transmission, diffuse reflectance, transreflectance, ATR.
- 19) A method as in Claim 14, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in at least one of transmission, diffuse reflectance, transreflectance, ATR.
- 20) A method as in Claim 14, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 4000 – 25000  $\text{cm}^{-1}$ .
- 21) A method as in Claim 14, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 4000 – 8000  $\text{cm}^{-1}$ .
- 22) A method as in Claim 14, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation in the spectral frequency range from 6000 – 6500  $\text{cm}^{-1}$ .
- 23) A method as in Claim 14, wherein determining an infrared spectrum comprises measuring the sample absorbance of infrared radiation at a spectral resolution of 64  $\text{cm}^{-1}$  or finer.
- 24) A method as in Claim 14, wherein determining the concentration of hemoglobin comprises at least one of:
  - a) Direct measurement of a blood sample using an external instrument or method;
  - b) Spectroscopic measurement of a blood sample; and
  - c) Noninvasive measurement of perfused tissue.
- 25) A method as in Claim 14, wherein determining the concentration of hemoglobin comprises at least one of:
  - a) Measuring the sample hemoglobin concentration under physiological conditions that are not undergoing rapid change;
  - b) Accounting for errors introduced by potentially interfering intravascular substances.
- 26) A method as in Claim 14, wherein the sample comprises at least one of:
  - a) A blood sample drawn from the patient;
  - b) A blood sample measured intravascularly (indwelling measurement);
  - c) Perfused tissue;
  - d) Perfused skin;
  - e) An ex vivo blood sample in a transmission vessel;
  - f) An ex vivo blood sample in a transreflectance vessel;

- g) A blood sample in an on-line flow circuit;
  - h) In situ measurement of a perfused tissue; and
  - i) In situ measurement of a perfused organ or muscle.
- 27) An apparatus for determining the pH of a sample, comprising:
- a) An illumination system adapted to direct radiation to the sample;
  - b) A collection system adapted to receive radiation expressed from the sample responsive to incident radiation;
  - c) An analysis system, comprising a model relating two or more of radiation expressed, incident radiation, and hemoglobin concentration to sample pH.
- 28) An apparatus as in Claim 27, wherein:
- a) The infrared radiation encompasses the spectral frequency range between 4000 – 25000 cm<sup>-1</sup>;
  - b) Infrared radiation is delivered to the sample through at least one of: optical fibers, light guides, and imaging optics;
  - c) Hemoglobin concentration is determined using radiation in the spectral frequency range from 10,000 – 25,000 cm<sup>-1</sup>; and
  - d) pH is determined using radiation in the spectral frequency range from 4,000 – 10,000 cm<sup>-1</sup> combined with the hemoglobin concentration.
- 29) An apparatus for determining the pH of a sample, comprising:
- a) Means for determining an infrared spectrum of the sample;
  - b) Means for determining the concentration of hemoglobin of the sample;
  - c) Means for selecting a model relating an infrared spectrum to pH that is applicable for samples having the determined hemoglobin concentration;
  - d) Means for determining the pH of the sample from the infrared spectrum and the selected model.